REMARKS

In the Office Action dated August 23, 2006, claims 21-76 and 79-100 are pending in the application. The Examiner has made the Restriction Requirement final. Consequently, claims 21-75 and 98-100 are withdrawn from consideration. Claims 76 and 79-97 are under examination. Claims 76 and 79-97 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support in the specification. Claims 76 and 79-97 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Xu et al. (U.S. 2002/0072117 A1). Claims 76 and 79-97 are also rejected under 35 U.S.C. §102(e) as allegedly anticipated by Xu (U.S. Patent No. 6,642,048 B2). Claims 76 and 79-97 are further rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bodnar et al. (WO 99/20740) in view of Bongso et al. (*Hum. Reprod.* 9 (11): 2110-2117 (1994)). The application is also objected to for failing to comply with the sequence rules set forth in 37 C.F.R. §§1.821-1.825. Additionally, the Examiner alleges that certified copies of the priority documents have not been filed.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

With respect to the priority claim, the Examiner has acknowledged Applicant's claim of priority to Australian Applications PR8028. PS0789 and PS1812, and states that certified copies of the priority documents have not been filed.

Applicants respectfully submit that in additional to PR8028. PS0789 and PS1812, the present application also claims priority to Australian Application PS2364, as stated in the submission dated March 29, 2004. Further, certified copies of all four priority documents were filed with the Patent Office on May 27, 2004. As evidence, Applicants provide herewith a copy

of Applicants' Claim of Priority dated May 27, 2004, and a copy of the returned post card with a date stamp from the Patent Office.

With respect to the objection to the application under 37 C.F.R. §§1.821-1.825, Applicants have amended the specification to insert the appropriate sequence identifiers for sequences already included in the Sequence Listing. In view of the amendment to the specification, the objection under 37 C.F.R. §§1.821-1.825 is overcome and withdrawal thereof is respectfully requested.

Claims 76 and 79-97 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support in the specification. Specifically, the Examiner alleges that the specification does not provide enablement for using any feeder cell layer, other than a fibroblast feeder cell, to condition the medium in order to derive and culture an ES cell line in an undifferentiated state.

Applicants have amended independent claim 76 to define the feeder layer as a fibroblast feeder cell layer comprising human adult fibroblast feeder cells. Applicants respectfully submit that the rejection is obviated in light of the amendment to the claims. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 76 and 79-97 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Xu et al. (U.S. 2002/0072117 A1). Claims 76 and 79-97 are also rejected under 35 U.S.C. §102(e) as allegedly anticipated by Xu (U.S. Patent No. 6,642,048 B2). It is observed that the underlying application of the '117 publication claims priority from Serial No. 09/900,752, which issued as the '048 patent.

Applicants respectfully submit that, as presently recited, the claims are directed to conditioned media by culturing a fibroblast feeder layer comprising human *adult* fibroblast

feeder cells. In dependent claims, the human *adult* fibroblast feeder cells are selected from adult skin fibroblast feeder cells, adult muscle fibroblast feeder cells, or HAFT fibroblast feeder cells, all of which are derived from adult (new born and older) primary tissue and are untransformed cells.

With respect to the '117 publication, the Examiner alleges that the reference teaches a medium conditioned by *fibroblast-like* cells, which are derived from human ES cells (Paragraph 0036 of the '117 publication). Similarly, with respect to the '048 patent, the Examiner alleges that the reference teaches that the cells used to prepare a conditioned medium can be a human cell line that has the characteristic of a human muscle or fibroblast cell, also referred to in the '048 patent as a *fibroblast-like* cell.

Applicants respectfully submit that the human "fibroblasts-like cells", referred to in both references, are disclosed as derived from human ES cells, in contrast to human *adult* fibroblast feeder cells employed in the present claims. The hES derived fibroblast-like cells of both references have not been exposed to surrounding tissues as would the *adult* fibroblast feeder cells. Notably, it is stated in the '117 publication on page 3, paragraph 0034, that "[f]ibroblasts derived from adults are generally not used as feeder cells, suggesting that more mature cells lose the ability to provide the factors requisite to support stem cell growth." (Emphasis added.) This statement in the '117 publication itself supports the notion that *adult* fibroblast feeder cells are different from the hES derived fibroblasts-like cells of both the '117 publication and the '048 patent.

In view of the foregoing, it is respectfully submitted that neither the '117 publication nor the '048 patent teaches the conditioned medium, as presently claimed. As such, the

rejections under 35 U.S.C. §102(e) based on the '117 publication and the '048 patent, respectively, are overcome. Withdrawal of the rejections is respectfully requested.

Claims 76 and 79-97 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bodnar et al. (WO 99/20740) in view of Bongso et al. (*Hum. Reprod.* 9 (11): 2110-2117 (1994)).

The Examiner states that Bodnar et al. teach the growth of primate-derived primordial stem cells by culturing the cells in a nutrient medium, and a substrate consisting of feeder cells and an extracellular matrix component. The Examiner alleges that Bodnar et al. also teach making a conditioned medium by supplementing with soluble factors derived from feeder cells. The Examiner has admitted that Bodnar et al. do not specifically teach using a human feeder cell for conditioning the media. However, the Examiner contends that Bongso et al. teach the development of human embryos to blastocyst stage on human tubal epithelial monolayers, and then after blastocyst formation, the hatched ICM and trophoblast were allowed to attach to the feeder monolayer. The Examiner's reasoning seems to be that since ICM contains ES cells and ICM was cultured on a human feeder monolayer, Bongso et al. inherently teach culturing ES cells on a human feeder layer. Therefore, the Examiner concludes that it would have been obvious to combine the teachings of the two references to arrive at the presently claimed invention.

Applicants respectfully submit that the claims have been amended to refer to human adult fibroblast feeders. As conceded by the Examiner, Bodnar et al. do not specifically teach using a human feeder cell for conditioning the media. Therefore, the teaching of Bodnar et al. is no longer relevant to the instant claims.

Furthermore, Applicants respectfully submit that the conditioned media of the present invention is capable of supporting the derivation and the culture of a pluripotent hES cell line and maintaining the cells in an undifferentiated state. Bongso et al. were only able to maintain the ICM-derived cells in a stem cell like morphology for two passages. This is not a cell line, as recited in the present claims.

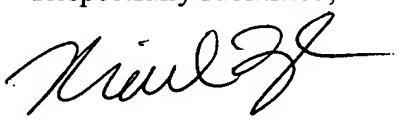
Moreover, the Examiner's reliance on Bongso et al. appears to be premised on the assumption that ICM lumps of Bongso et al. equate to ES cells in the context of the present invention. Applicants respectfully submit that such assumption is erroneous. ICM lumps include other cell types that may assist in maintaining those cells with a stem cell like morphology. The ICM comprises cells that are destined to become the embryo, which is a mass of different cell types. The present invention relates to providing a "cell line", which by definition is a pure cell type cultured in the absence of other cell types. Moreover, the cell line referenced in the present claims is an ES cell line, which has defined stem cell morphology.

Additionally, Applicants observe that in Bongso et al., two of the ICM lumps differentiated into fibroblast cells, in contrast to the present claims, which are directed to a conditioned medium specifically for deriving and culturing an ES cell line in a substantially undifferentiated state. Therefore, those skilled in the art would not have gained any motivation from the Bongso reference to modify the method of Bodnar et al., as Bongso would not have provided one skilled in the art with any reasonable expectation of success in attempting to arrive at the present invention. Applicants respectfully submit that there is no teaching in the Bongso reference that the feeder layers had any contribution to maintaining the cells in an undifferentiated state, much less a teaching for a conditioned media derived from the feeders that would maintain the cells in an undifferentiated state.

Accordingly, Applicants respectfully submit that Bodnar et al. and Bongso et al., taken singularly or in combination, fail to provide those skilled in the art with the requisite motivation and a reasonable expectation of success in order to render the presently claimed invention obvious. Thus, the rejection under 35 U.S.C. §103(a) based on the combination of Bodnar et al. and Bongso et al. is overcome. Withdrawal of the rejection is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Enc.: Copies of the May 27, 2004 submission and return post card